SciLifeLab

Name or type of instrument	MESO SECTOR S 600MM electrochemiluminescence plate reader
Unit	Affinity Proteomics Uppsala
Platform	Clinical Proteomics and Immunology
Applicant (Head of Unit)	Mikael Åberg
E-mail address	mikael.aberg@medsci.uu.se
Instrument, acquisition cost (kSEK)	2300
Funding applied for (kSEK)	1800

Description of the instrument

The MesoScale Discovery (MSD) System is a versatile platform that finds its application throughout all phases of biological research. It is an excellent system to detect cytokines, chemokines, antibodies and other biomarkers as well as therapeutic antibody-antigen interactions for affinity determinations and potency estimations with high sensitivity and broad dynamic range. Similar to conventional ELISA, the MSD platform delivers weight to volume data but has the advantage of being a multiplexing technique ideally suited to supporting time- and resource-saving laboratory procedures. As a trained core lab, we have offered service for this technology since 2018. Owing to the increasing demand we now want to upgrade to a new and better instrument and in parallel introduce a more automated workflow. This application concerns the acquisition of the MESO SECTOR S 600MM plate reader.

Technology: Plate-based ElectroChemical Luminescence (ECL) is proprietary to MSD and they are the only company that manufactures and sells instruments and reagents for this technology which facilitates the procurement. However, it is an open platform that allows us and other users to develop our own assays as a complement to the already available assays. The analysis software is furthermore free to download for users who wants to analyze their own data or go beyond our curated reports. The multi-spot plates are available in 96- and 384 -well formats with up to 10 array spots per well.

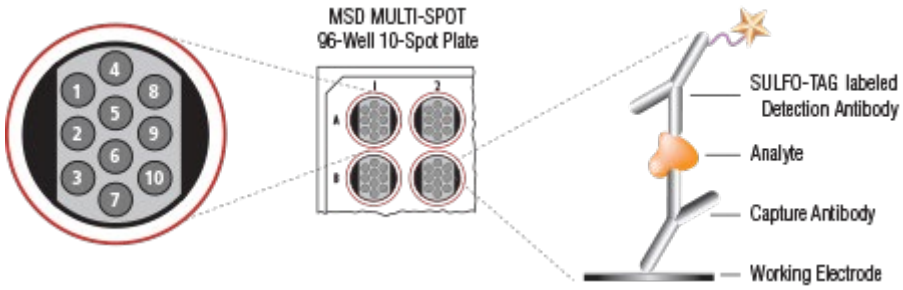

Figure 1. Working principle of the assay. ©MSD

The high binding carbon electrodes of the assay plate enables easy attachment of a broad variety of reagents including antibodies and non-antibody molecules (carbohydrates, virus-like particles, peptides and membrane lysates). The surface is even eligible for spreading of living cells. The MSD SULFO-TAG label can be easily conjugated to any detection antibody and there are off the shelf species-specific SULFO-TAG™ conjugated antibodies that we have used for e.g. customized covid-19 antibody tests.

When the detection antibody comes in close proximity to the plate electrodes and electricity is applied, a series of reduction and oxidation reactions are set in motion. This results in light emission at approximately 620 nm and allows quantitative measurement of analytes in the sample. Since the detection is based on electricity in and light out, the background is very low and the sensitivity allows high dilution factors which remove matrix effects to purify the signal even further. The dynamic range is typically 3-4 logs and most assays have a sensitivity in the low pg/ml range, some even down to fg/ml (the so-called S-plex line). The matrix tolerance is high and we have analyzed several complex sample types such as serum, plasma, tissue lysates, CSF, BAL, sputum etc.

Instrument: We currently have SQ 120MM reader installed. It is the entry levels instrument suited for individual research groups or core labs with fewer projects. It has overall functioned well but the analysis of +1000 plates during 2021-22 in <50 projects has left its mark. After installation of a new instrument it will still function as a backup and, as before, we will continue to lend it to research groups that prefer to do their own wet work in the 96-well format. The MESO SECTOR S 600MM is the next-level MSD flagship plate reader in the SECTOR instruments product line. It has been developed under design control and validated through MSD's quality management system. As compared to the SQ120, the S600MM employs an upgraded, ultra-low-noise, CCD camera system, improved electronics for better performance and built-in plate barcode readers. It features custom-designed telecentric lenses for rapid detection (50 plates/hour) using all MULTI ARRAY or MULTI SPOT plates. It also has the capability to analyze 384-well plates with all the benefits that this brings and will, under supervision, be available for external users with their own plates againts a small fee.

Figure 2. Comparison between the Sector S 600MM (left) and QuickPlex SQ 120MM. The foot print of the S600MM is somewhat larger than the SQ120MM but it still fits on a conventional lab bench. ©MSD

Statement of need

During the last years we have received both Covid and non-Covid projects with challenging demands when it comes to turn around time and samples size. Data has been delivered but these types of projects have required much valuable hands-on labor. It is our belief that several of these projects, with slight modifications, could have been performed using a 384-well format instead. A number of similar projects are planned during 2023 with e.g. the Public Health Agency of Sweden as users.

MSD's U-PLEX system allows us and other users to create custom multiplex assays for any combination of analytes using two simple tools: A U-PLEX plate and unique linkers. In U-PLEX assays, biotinylated capture reagents are coupled to the linkers. The linkers then self-assemble onto unique spots on the U-PLEX plate. After analytes in the sample bind to the capture reagents, detection antibodies conjugated with SULFO-TAG labels bind to the analytes to complete the sandwich immunoassay. In addition to antibodies, U-PLEX is designed to be used with other readily available biotin-conjugated reagents including peptides, proteins, and nucleic acids. With start in September 2022, these types of assays are also available for 384-well plates. The reduction in consumables and sample volume combined with a 75% reduction in reagents means cheaper, faster and more environmentally friendly analyses. With the S600MM we would thus get a 384-plate based multiplex tool for discovery or validation cohorts, stemming from technologies such as Olink Explore, that would save both time and money for all parties involved.

There is an emerging insight that the snapshot of the broad immune response mirrored in serum or plasma analyses answer one type of questions and the specific mucosal response measured in e.g. nasal swabs others. As of late we therefore also moved into a new type of Covid analyses beyond the very successful high-throughput serum analyses we have provided since 2021. We recently published a study where we looked at antibodies in the nasal mucosa (Anti-Spike Mucosal IgA Protection against SARS-CoV-2 Omicron Infection | NEJM) and have during the summer analyzed almost a thousand saliva samples in the Covaxid study (https://clinicaltrials.gov/ct2/show/NCT04780659). The main challenge is that the antibody levels are much lower in these types of matrixes than in serum/plasma. We now get new requests to find mucosa specific or neutralizing antibodies and to measure post-translational modifications and different subclasses of IgG and IgA. These subsets are even lower in concentration, also in serum/plasma, and we must therefore use lower dilution factors and with the basis in MSD's variant screening panels (MSD Assays for COVID-19 Research | Meso Scale Discovery) take benefit from the open system and further develop the panels. This is frontline research and we believe that the better camera system in the S600MM systems would greatly aid in these types of studies where analyses are performed closer to the noise level. With the forthcoming introduction of nasal covid-19 vaccines, currently in clinical trials, the importance of studying these types of low-level samples with good resolution between both variants and treated groups will increase.

Finally, the S600MM have two internal barcode readers. The barcode information allows the analysis software to identify the plate and to read and interpret the data correctly and it is also possible to add user specific barcodes to the plates. Today, we must add all information about the plates and assays manually and this automatic step would reduce both the chance of error and time spent in front of the instrument. This also fits well with ideas within CPI in going toward a more regulated/standardized lab environment.

Co-funding: The unit will co-fund up to 500k SEK for the purchase of the MESO SECTOR S 600MM and has set aside funds for the transition from hand pipetting to automation, a necessary step for the 384-plate analyses. A wash robot has already been installed and several pipetting systems are being evaluated. The service agreements for the plate reader and robots and the deprication of the robots will be covered by future user fees.